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Title

IS A POST-SURGE DROP IN ESTRADIOL SIGNIFICANT IN FREEZE-ALL CYCLES?

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Objective

Fresh IVF cycle studies have shown that a significant post-trigger fall in estradiol (E2) may be associated with lower pregnancy rates. It is not clear whether the deleterious effect is related to the increased incidence of this phenomenon in patients with diminished ovarian reserve, to specific defects in the oocyte or follicular apparatus, or to an endometrial effect. This study sought to evaluate whether a significant post-surge fall in E2 is ultimately associated with diminished implantation following oocyte fertilization, and biopsy vitrification and rewarming of the embryo

Design

Retrospective cohort study.

Materials and Methods

This study includes patients undergoing fresh IVF cycles with PGT who experienced a drop in E2 on the day after surge (Day+1) and had a subsequent single, euploid FET from 2012-2017. Patients were grouped by percentage decrease in E2 on Day+1 (<5%, 5-10%, >10%). A secondary analysis included the degree of luteinization based on percentage rise in progesterone (P4) on Day+1 (<80% or ≥80%). Implantation was confirmed by the presence of an intrauterine gestational sac on ultrasound. Ongoing pregnancy rate (OPR) and early pregnancy loss rate (EPL) were determined. Data was analyzed with a student's t-test and chi-squared. A binary



logistic regression and ROC curve were used to calculate youden’s index (j-statistic) to determine the degree of P4 rise that signified luteinization.

Results

A total of 788 fresh IVF cycles and 366 single, euploid FET cycles with a decrease in E2 on Day+1 were performed. Patients with an E2 drop had a lower blastulation rate ( $5.21 \pm 4.2$  vs.  $5.86 \pm 4.9$ ,  $p < 0.001$ ) and had fewer euploid embryos ( $1.95 \pm 2.34$  vs.  $2.38 \pm 2.73$ ,  $p < 0.001$ ) than those who did not. In patients undergoing FET, no difference in patient age, BMI, ovarian reserve outcome, peak E2, number of oocytes retrieved or number of embryos ongoing on Day 1 was observed regardless of level of E2 decline. Patients shown to have the greatest decrease in E2 required a higher dose of gonadotropins (GND) during stimulation ( $>10\%$  E2 drop  $4221 \pm 1339$  vs  $5-10\%$   $3693 \pm 1324$  vs.  $<5\%$   $3911 \pm 1453$ ,  $p=0.01$ ). Implantation rate, OPR and EPL did not differ among groups even after comparing degree of luteinization [Table 1].

Conclusions

While cycles notable for a post-surge fall in E2 were less likely to produce an embryo suitable for FET, if a euploid embryo was identified, pregnancy outcome was not affected. These results separate out the stimulation from the transfer processes, and conclude that a post-surge fall in E2 should not be used as an indicator for cycle cancellation.

Support

None.

Table 1.

Cycle Parameters and IVF Outcomes based on Percent Drop in Estradiol Level

	E2 Decline $<5\%$ (n=135)	E2 Decline $\geq 5 \leq 10\%$ (n=96)	E2 Decline $>10\%$ (n=135)	P Value
Age (y)	$37.1 \pm 3.85$	$36.8 \pm 3.75$	$36.9 \pm 3.88$	NS
BMI ( $\text{kg}/\text{m}^2$ )	$22.3 \pm 3.06$	$22.0 \pm 2.95$	$22.1 \pm 3.76$	NS
Day 3 FSH (IU/mL)	$6.04 \pm 2.82$	$6.29 \pm 3.92$	$6.66 \pm 4.04$	NS
AMH (pmol/L)	$2.64 \pm 2.15$	$2.76 \pm 2.01$	$2.58 \pm 2.36$	NS
Basal Antral Follicle Count	$11.4 \pm 5.04$	$10.6 \pm 6.21$	$10.1 \pm 4.74$	NS



Total GND	3911 ± 1453	3693 ± 1324	4221 ± 1339	0.01
Peak E2 (pg/mL)	2473 ± 1208	2409 ± 1195	2354 ± 1071	NS
#oocytes retrieved	15.6 ± 7.86	14.2 ± 7.70	13.7 ± 7.65	NS
#embryos D1	10.4 ± 5.75	9.62 ± 5.52	8.95 ± 5.08	NS
#embryos D5	7.39 ± 4.76	6.37 ± 4.52	6.44 ± 4.33	NS
EM thickness on day of transfer (mm)	9.08 ± 1.46	10.0 ± 2.59	9.35 ± 1.72	0.001
Day 5 Embryo Transfer	92/135 = 68.1%	63/96 = 65.6%	91/135 = 67.4%	NS
Implantation Rate	81/135 = 60%	61/96 = 63.5%	79/135 = 58.5%	NS
IR (P4 rise ≥ 80%)	43/67 = 64.2%	30/45 = 66.7%	35/59 = 59.3%	NS
IR (P4 rise <80%)	38/68 = 55.9%	31/51 = 60.8%	44/76 = 57.9%	NS
Ongoing Pregnancy Rate	73/135 = 54.1%	48/96 = 50%	66/135 = 48.9%	NS
OPR (P4 rise ≥ 80%)	37/67 = 55.2%	26/45 = 57.8%	30/59 = 50.8%	NS
OPR (P4 rise <80%)	36/68 = 52.9%	22/51 = 43.1%	36/76 = 47.4%	NS
Early Pregnancy Loss	24/135 = 17.8%	20/96 = 20.8%	27/135 = 20%	NS
EPL (P4 rise ≥ 80%)	15/67 = 22.4%	8/45 = 17.8%	10/59 = 16.9%	NS
EPL (P4 rise <80%)	9/68 = 13.2%	12/51 = 23.5%	17/76 = 22.4%	NS